FIGURE 1

```
   1  ATGTCAGTGGGAGCCATGAAGAAGGGAGTGGGGAGGGCAGTTGGGCTTGGAGGCGGCAGC   60
  61  GGCTGCCAGGCTACGGAGGAAGACCCCCTTCCCGACTGCGGGGCTTGCGCTCCGGGACAA  120
 121  GGTGGCAGGCGCTGGAGGCTGCCGCAGCCTGCGTGGGTGGAGGGGAGCTCAGCTCGGTTG  180
 181  TGGGAGCAGGCGACCGGCACTGGCTGGATGGACCTGGAAGCCTCGCTGCTGCCCACTGGT  240
 241  CCCAATGCCAGCAACACCTCTGATGGCCCCGATAACCTCACTTCAGCAGGATCACCTCCT  300
 301  CGCACGGGGAGCATCTCCTACATCAACATCATCATGCCTTCGGTGTTCGGCACCATCTGC  360
 361  CTCCTGGGCATCATCGGGAACTCCACGGTCATCTTCGCGGTCGTGAAGAAGTCCAAGCTG  420
 421  CACTGGTGCAACAACGTCCCCGACATCTTCATCATCAACCTCTCGGTAGTAGATCTCCTC  480
 481  TTTCTCCTGGGCATGCCCTTCATGATCCACCAGCTCATGGGCAATGGGGTGTGGCACTTT  540
 541  GGGGAGACCATGTGCACCCTCATCACGGCCATGGATGCCAATAGTCAGTTCACCAGCACC  600
 601  TACATCCTGACCGCCATGGCCATTGACCGCTACCTGGCCACTGTCCACCCCATCTCTTCC  660
 661  ACGAAGTTCCGGAAGCCCTCTGTGGCCACCCTGGTGATCTGCCTCCTGTGGGCCCTCTCC  720
 721  TTCATCAGCATCACCCCTGTGTGGCTGTATGCCAGACTCATCCCCTTCCCAGGAGGTGCA  780
 781  GTGGGCTGCGGCATACGCCTGCCCAACCCAGACACTGACCTCTACTGGTTCACCCTGTAC  840
 841  CAGTTTTTCCTGGCCTTTGCCCTGCCTTTTGTGGTCATCACAGCCGCATACGTGAGGATC  900
 901  CTGCAGCGCATGACGTCCTCAGTGGCCCCCGCCTCCCAGCGCAGCATCCGGCTGCGGACA  960
 961  AAGAGGGTGACCCGCACAGCCATCGCCATCTGTCTGGTCTTCTTTGTGTGCTGGGCACCC 1020
1021  TACTATGTGCTACAGCTGACCCAGTTGTCCATCAGCCGCCCGACCCTCACCTTTGTCTAC 1080
1081  TTATACAATGCGGCCATCAGCTTGGGCTATGCCAACAGCTGCCTCAACCCCTTTGTGTAC 1140
1141  ATCGTGCTCTGTGAGACGTTCCGCAAACGCTTGGTCCTGTCGGTGAAGCCTGCAGCCCAG 1200
1201  GGGCAGCTTCGCGCTGTCAGCAACGCTCAGACGGCTGACGAGGAGAGGACAGAAAGCAAA 1260
1261  GGCACCTGA                                                     1269
```

FIGURE 2

1	M	S	V	G	A	M	K	K	G	V	G	R	A	V	G	L	G	G	G	S	20
21	G	C	Q	A	T	E	E	D	P	L	P	D	C	G	A	C	A	P	G	Q	40
41	G	G	R	R	W	R	L	P	Q	P	A	W	V	E	G	S	S	A	R	L	60
61	W	E	Q	A	T	G	T	G	W	M	D	L	E	A	S	L	L	P	T	G	80
81	P	N	A	S	N	T	S	D	G	P	D	N	L	T	S	A	G	S	P	P	100
101	R	T	G	S	I	S	Y	I	N	I	I	M	P	S	V	F	G	T	I	C	120
121	L	L	G	I	I	G	N	S	T	V	I	F	A	V	V	K	K	S	K	L	140
141	H	W	C	N	N	V	P	D	I	F	I	I	N	L	S	V	V	D	L	L	160
161	F	L	L	G	M	P	F	M	I	H	Q	L	M	G	N	G	V	W	H	F	180
181	G	E	T	M	C	T	L	I	T	A	M	D	A	N	S	Q	F	T	S	T	200
201	Y	I	L	T	A	M	A	I	D	R	Y	L	A	T	V	H	P	I	S	S	220
221	T	K	F	R	K	P	S	V	A	T	L	V	I	C	L	L	W	A	L	S	240
241	F	I	S	I	T	P	V	W	L	Y	A	R	L	I	P	F	P	G	G	A	260
261	V	G	C	G	I	R	L	P	N	P	D	T	D	L	Y	W	F	T	L	Y	280
281	Q	F	F	L	A	F	A	L	P	F	V	V	I	T	A	A	Y	V	R	I	300
301	L	Q	R	M	T	S	S	V	A	P	A	S	Q	R	S	I	R	L	R	T	320
321	K	R	V	T	R	T	A	I	A	I	C	L	V	F	F	V	C	W	A	P	340
341	Y	Y	V	L	Q	L	T	Q	L	S	I	S	R	P	T	L	T	F	V	Y	360
361	L	Y	N	A	A	I	S	L	G	Y	A	N	S	C	L	N	P	F	V	Y	380
381	I	V	L	C	E	T	F	R	K	R	L	V	L	S	V	K	P	A	A	Q	400
401	G	Q	L	R	A	V	S	N	A	Q	T	A	D	E	E	R	T	E	S	K	420
421	G	T																			422

FIGURE 3

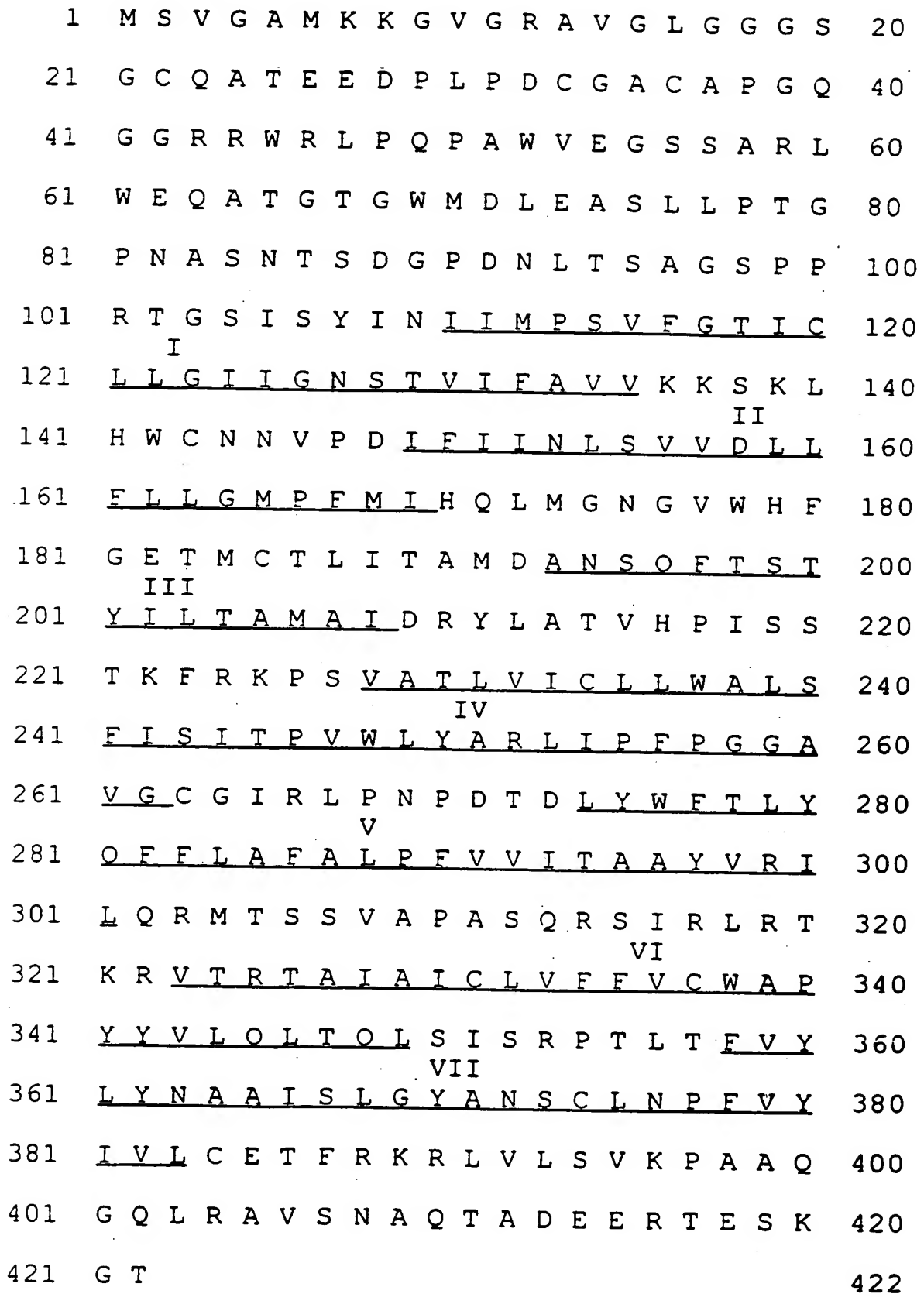


FIGURE 4

```
   1  GCAGGCGACCTGCACCGGCTGCATGGATCTGCAAACCTCGTTGCTGTCCACTGGCCCCAA   60
  61  TGCCAGCAACATCTCCGATGGCCAGGATAATCTCACATTGCCGGGGTCACCTCCTCGCAC  120
 121  AGGGAGTGTCTCCTACATCAACATCATTATGCCTTCCGTGTTTGGTACCATCTGTCTCCT  180
 181  GGGCATCGTGGGAAACTCCACGGTCATCTTTGCTGTGGTGAAGAAGTCCAAGCTACACTG  240
 241  GTGCAGCAACGTCCCCGACATCTTCATCATCAACCTCTCTGTGGTGGATCTGCTCTTCCT  300
 301  GCTGGGCATGCCTTTCATGATCCACCAGCTCATGGGGAACGGCGTCTGGCACTTTGGGGA  360
 361  AACCATGTGCACCCTCATCACAGCCATGGACGCCAACAGTCAGTTCACTAGCACCTACAT  420
 421  CCTGACTGCCATGACCATTGACCGCTACTTGGCCACCGTCCACCCCATCTCCTCCACCAA  480
 481  GTTCCGGAAGCCCTCCATGGCCACCCTGGTGATCTGCCTCCTGTGGGCGCTCTCCTTCAT  540
 541  CAGTATCACCCCTGTGTGGCTCTACGCCAGGCTCATTCCCTTCCCAGGGGGTGCTGTGGG  600
 601  CTGTGGCATCCGCCTGCCAAACCCGGACACTGACCTCTACTGGTTCACTCTGTACCAGTT  660
 661  TTTCCTGGCCTTTGCCCTTCCGTTTGTGGTCATTACCGCCGCATACGTGAAAATACTACA  720
 721  GCGCATGACGTCTTCGGTGGCCCCAGCCTCCCAACGCAGCATCCGGCTTCGGACAAAGAG  780
 781  GGTGACCCGCACGGCCATTGCCATCTGTCTGGTCTTCTTTGTGTGCTGGGCACCCTACTA  840
 841  TGTGCTGCAGCTGACCCAGCTGTCCATCAGCCGCCCGACCCTCACGTTTGTCTACTTGTA  900
 901  CAACGCGGCCATCAGCTTGGGCTATGCTAACAGCTGCCTGAACCCCTTTGTGTACATAGT  960
 961  GCTCTGTGAGACCTTTCGAAAACGCTTGGTGTTGTCAGTGAAGCCTGCAGCCCAGGGGCA 1020
1021  GCTCCGCACGGTCAGCAACGCTCAGACAGCTGATGAGGAGAGGACAGAAAGCAAAGGCAC 1080
1081  CTGACAATTCCCCAGTCGCCTCCAAGTCAGGCCACCCCATCAAACCGTGGGGAGAGATAC 1140
1141  TGAGATTAAACCCAAGGCTACCCTGGGAGAATGCAGAGGCTGGAGGCTGGGGGCTTGTAG 1200
1201  CAACCACATTCCAC                                                1214
```

FIGURE 5

1	M	D	L	Q	T	S	L	L	S	T	G	P	N	A	S	N	I	S	D	G	20
21	Q	D	N	L	T	L	P	G	S	P	P	R	T	G	S	V	S	Y	I	N	40
41	I	I	M	P	S	V	F	G	T	I	C	L	L	G	I	V	G	N	S	T	60
61	V	I	F	A	V	V	K	K	S	K	L	H	W	C	S	N	V	P	D	I	80
81	F	I	I	N	L	S	V	V	D	L	L	F	L	L	G	M	P	F	M	I	100
101	H	Q	L	M	G	N	G	V	W	H	F	G	E	T	M	C	T	L	I	T	120
121	A	M	D	A	N	S	Q	F	T	S	T	Y	I	L	T	A	M	T	I	D	140
141	R	Y	L	A	T	V	H	P	I	S	S	T	K	F	R	K	P	S	M	A	160
161	T	L	V	I	C	L	L	W	A	L	S	F	I	S	I	T	P	V	W	L	180
181	Y	A	R	L	I	P	F	P	G	G	A	V	G	C	G	I	R	L	P	N	200
201	P	D	T	D	L	Y	W	F	T	L	Y	Q	F	F	L	A	F	A	L	P	220
221	F	V	V	I	T	A	A	Y	V	K	I	L	Q	R	M	T	S	S	V	A	240
241	P	A	S	Q	R	S	I	R	L	R	T	K	R	V	T	R	T	A	I	A	260
261	I	C	L	V	F	F	V	C	W	A	P	Y	Y	V	L	Q	L	T	Q	L	280
281	S	I	S	R	P	T	L	T	F	V	Y	L	Y	N	A	A	I	S	L	G	300
301	Y	A	N	S	C	L	N	P	F	V	Y	I	V	L	C	E	T	F	R	K	320
321	R	L	V	L	S	V	K	P	A	A	Q	G	Q	L	R	T	V	S	N	A	340
341	Q	T	A	D	E	E	R	T	E	S	K	G	T	*							354

FIGURE 6

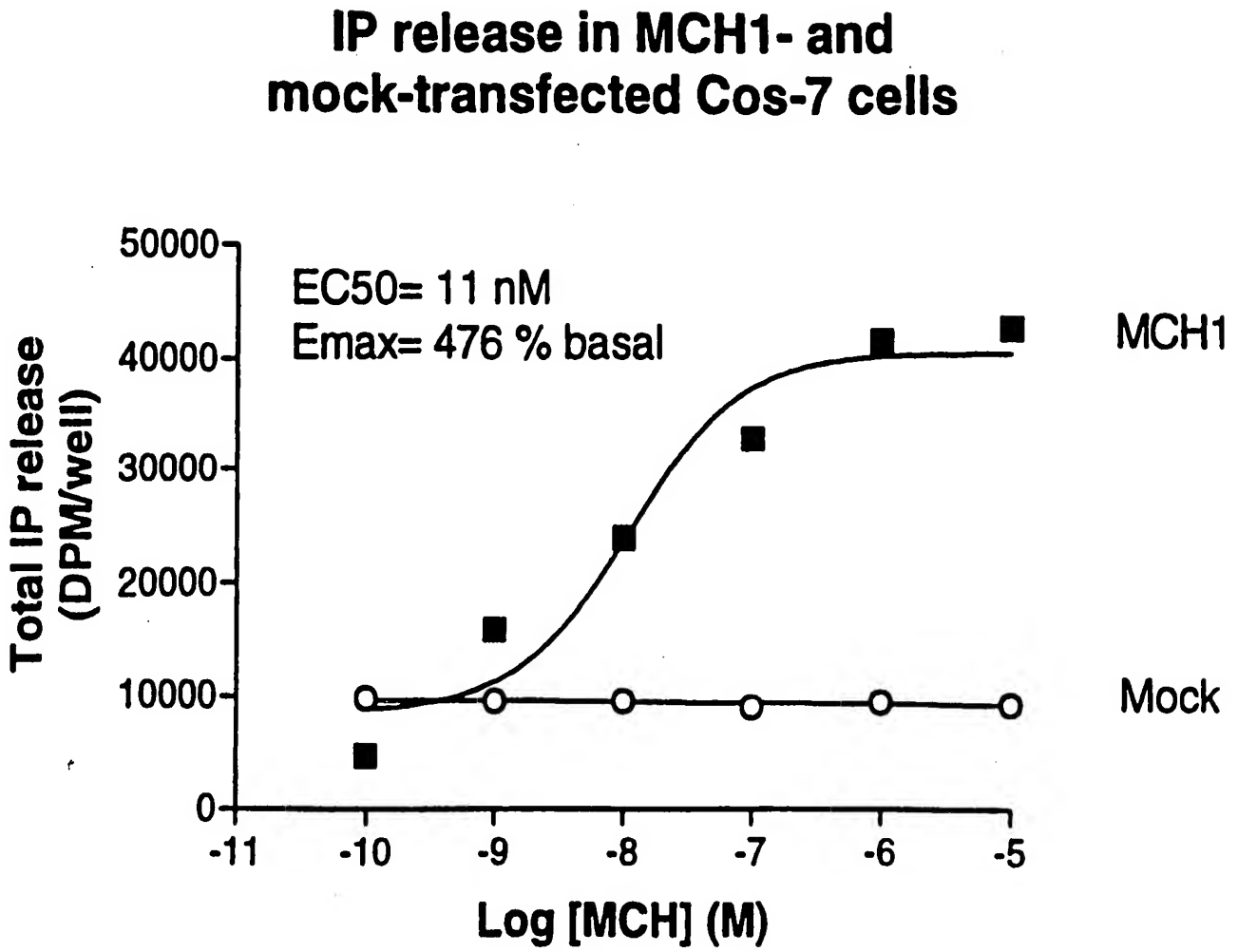


FIGURE 7

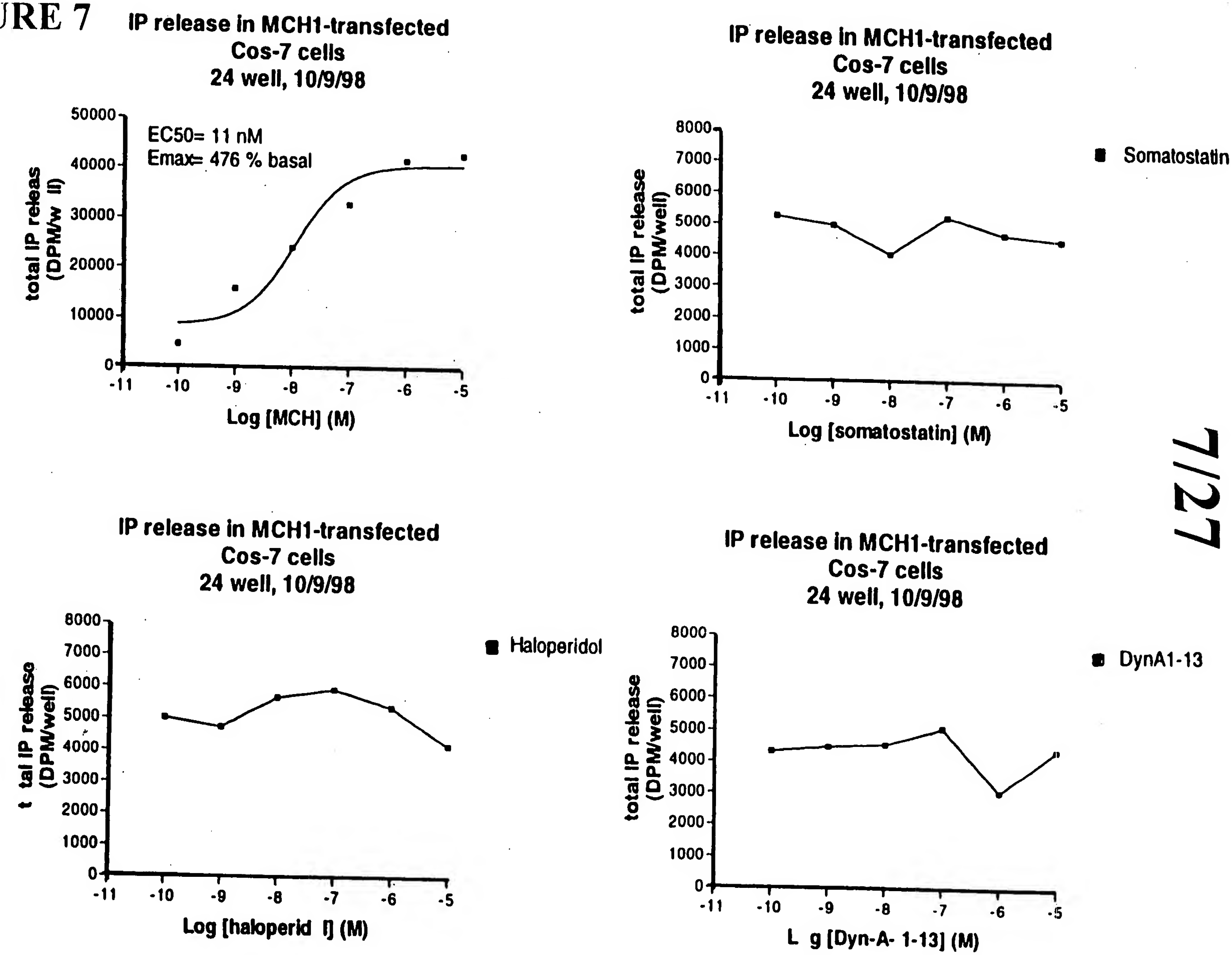
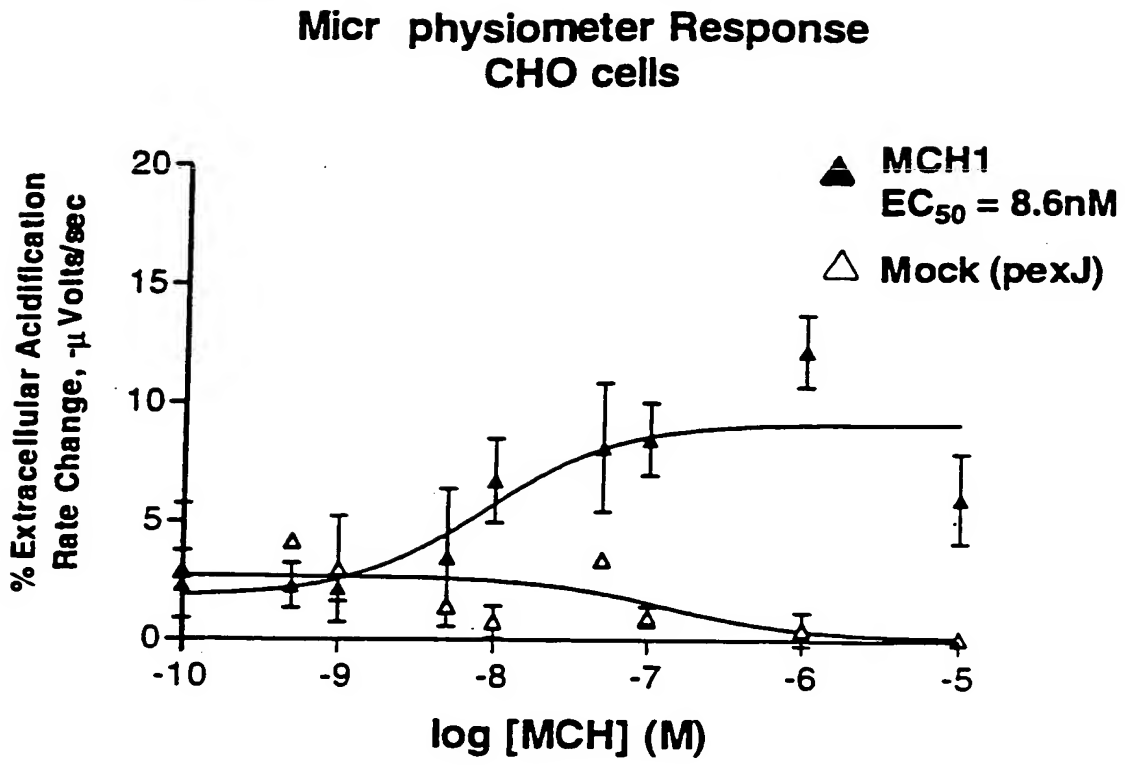


FIGURE 8


Micr physiometer Response
CHO cells
MCH1
EC50 = 8.6nM
Mock (pexJ)
% Extracellular Acidification Rate Change, -µ Volts/sec
20
15
10
5
0
-10
-9
-8
-7
-6
-5
log [MCH] (M)

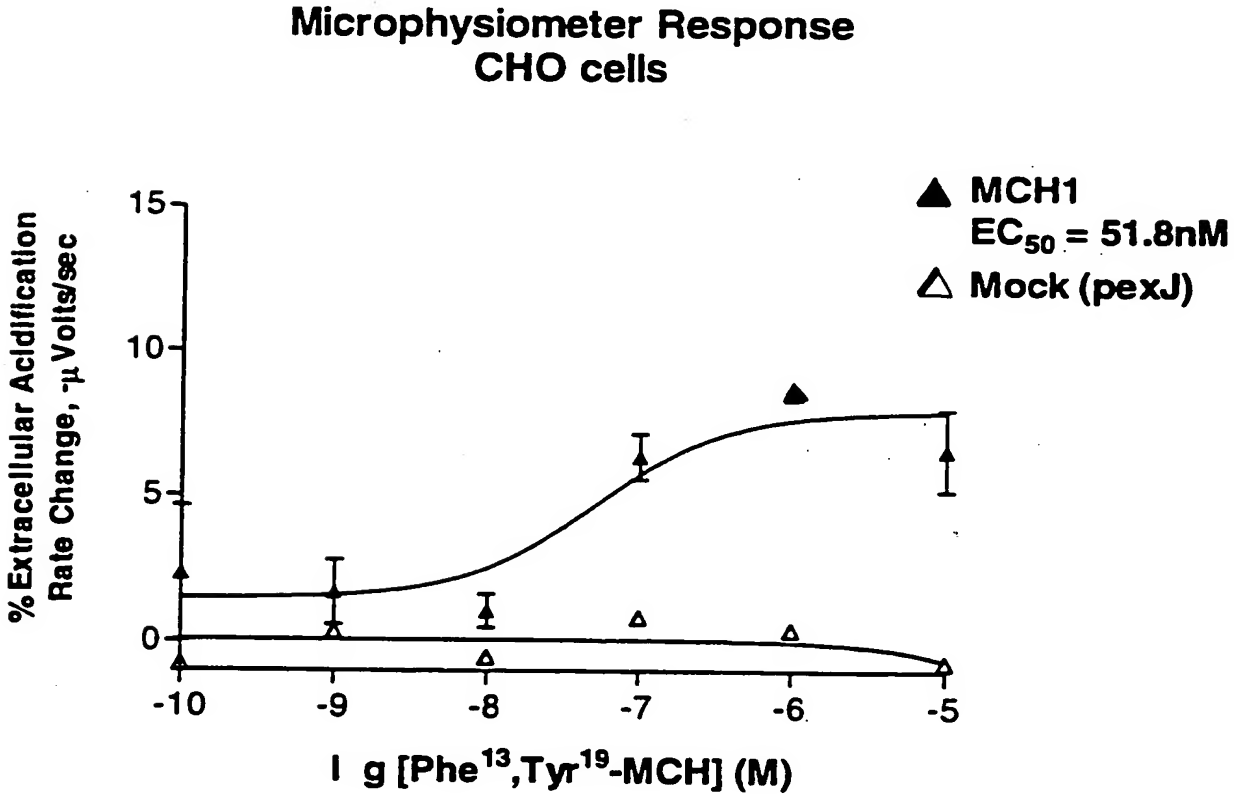

Microphysiometer Response
CHO cells
MCH1
EC50 = 51.8nM
Mock (pexJ)
% Extracellular Acidification Rate Change, -µ Volts/sec
15
10
5
0
-10
-9
-8
-7
-6
-5
l g [Phe13,Tyr19-MCH] (M)

FIGURE 9

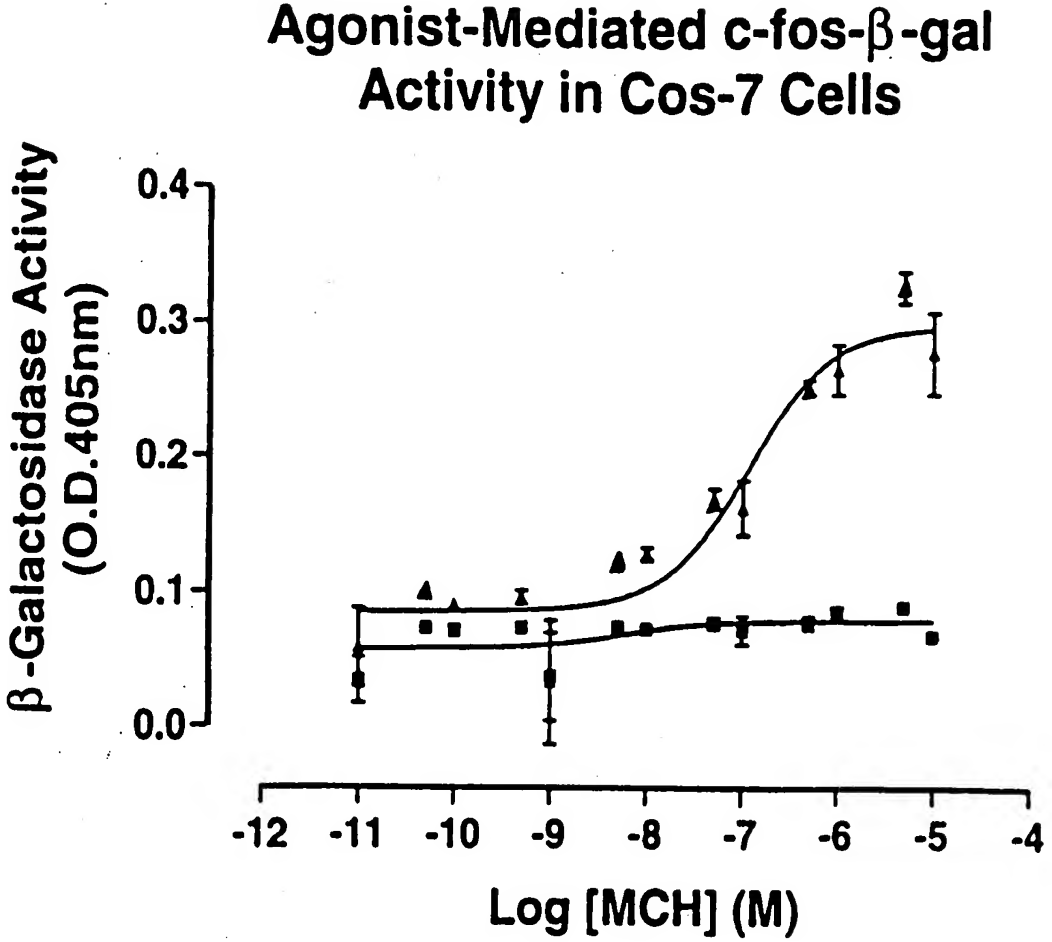
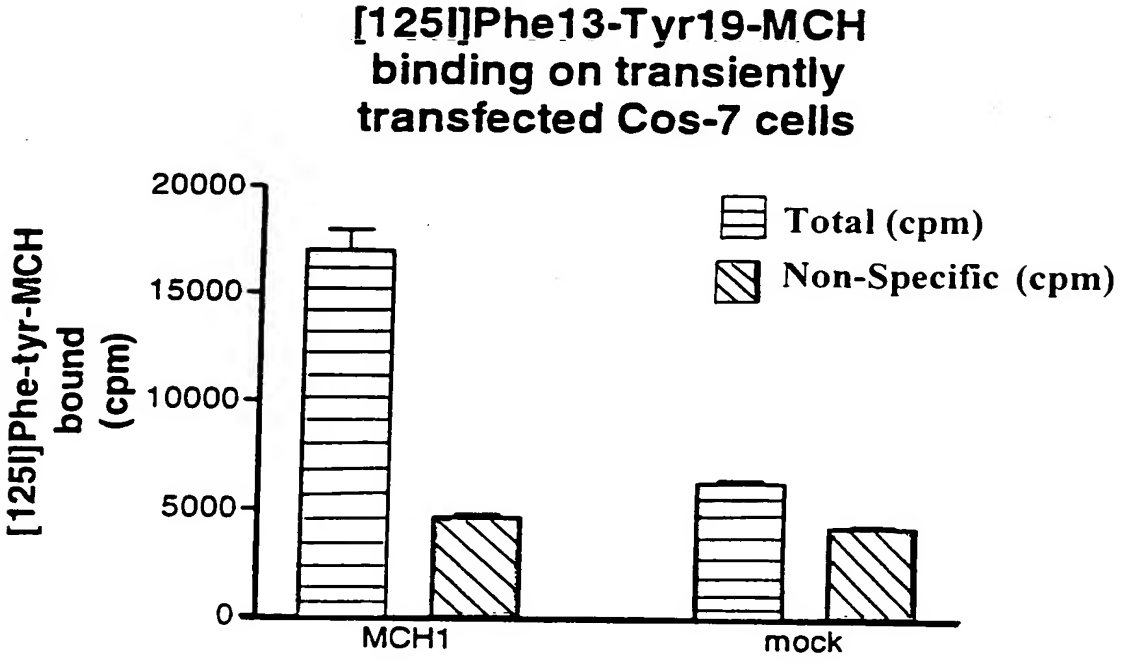


FIGURE 10



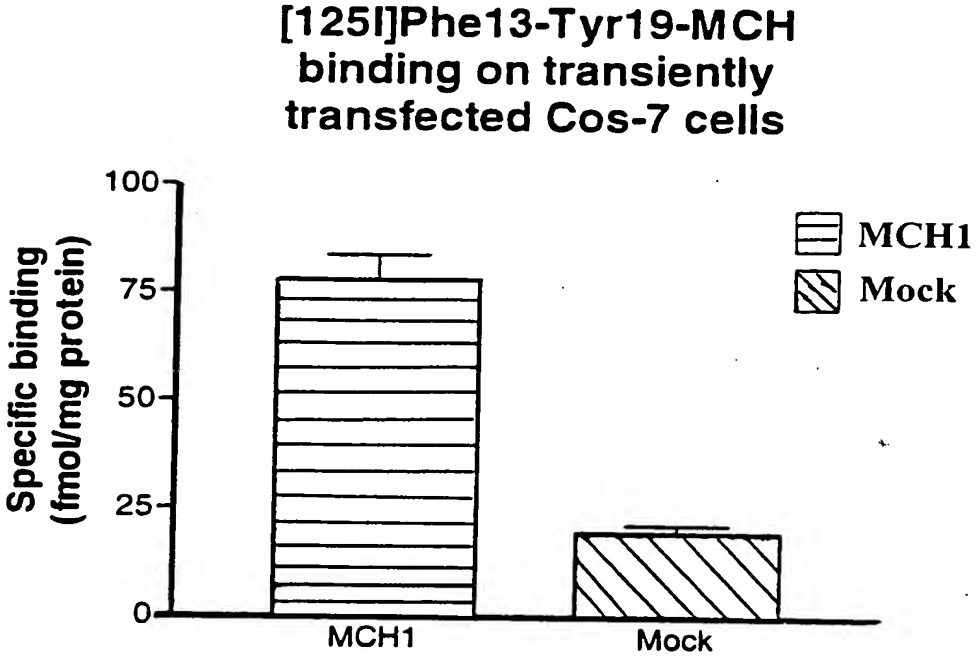


FIGURE 11

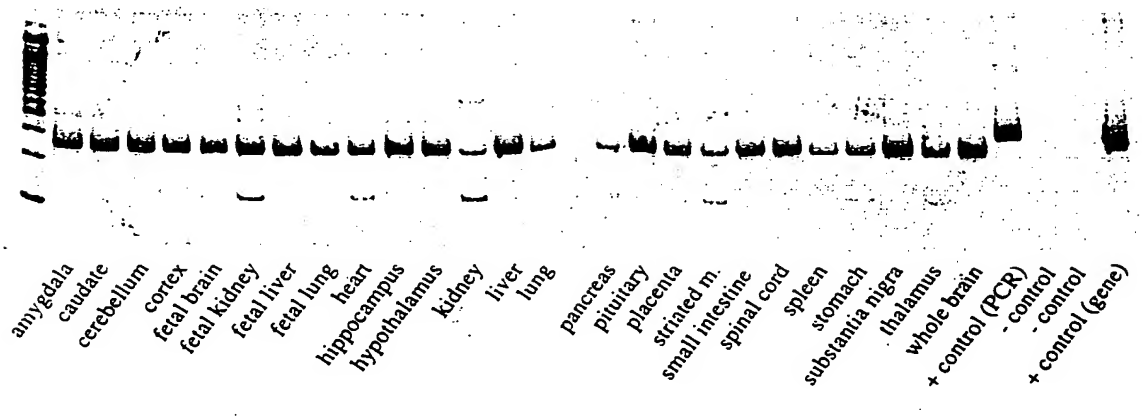

amygdala
caudate
cerebellum
cortex
fetal brain
fetal kidney
fetal liver
fetal lung
heart
hippocampus
hypothalamus
kidney
liver
lung
pancreas
pituitary
placenta
striated m.
small intestine
spinal cord
spleen
stomach
substantia nigra
thalamus
whole brain
+ control (PCR)
- control
- control
+ control (gene)

FIGURE 12

```
                1                                                  40
TL231   MSVGAMKKGV GRAVGLGGGS GCQATEEDPL PDCGACAQGQ
R106    MSVGAMKKGV GRAVGLGGGS GCQATEEDPL PDCGACAQGQ
R114    MSVGAaKKGV GRAVGLGGGS GCQATEEDPL PDCGACAQGQ
BO120   ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~

               41                                                  80
TL231   GGRRWRLPQP AWVEGSSARL WEQATGTGWM DLEASLLPTG
R106    GGRRWRLPQP AWVEGSSARL WEQATGTGWa DLEASLLPTG
R114    GGRRWRLPQP AWVEGSSARL WEQATGTGWa DLEASLLPTG
BO120   ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~M DLEASLLPTG

               81                                                 100
TL231   PNASNTSDGP DNLTSAGSPP...
R106    PNASNTSDGP DNLTSAGSPP...
R114    PNASNTSDGP DNLTSAGSPP...
BO120   PNASNTSDGP DNLTSAGSPP...
```

FIGURE 13

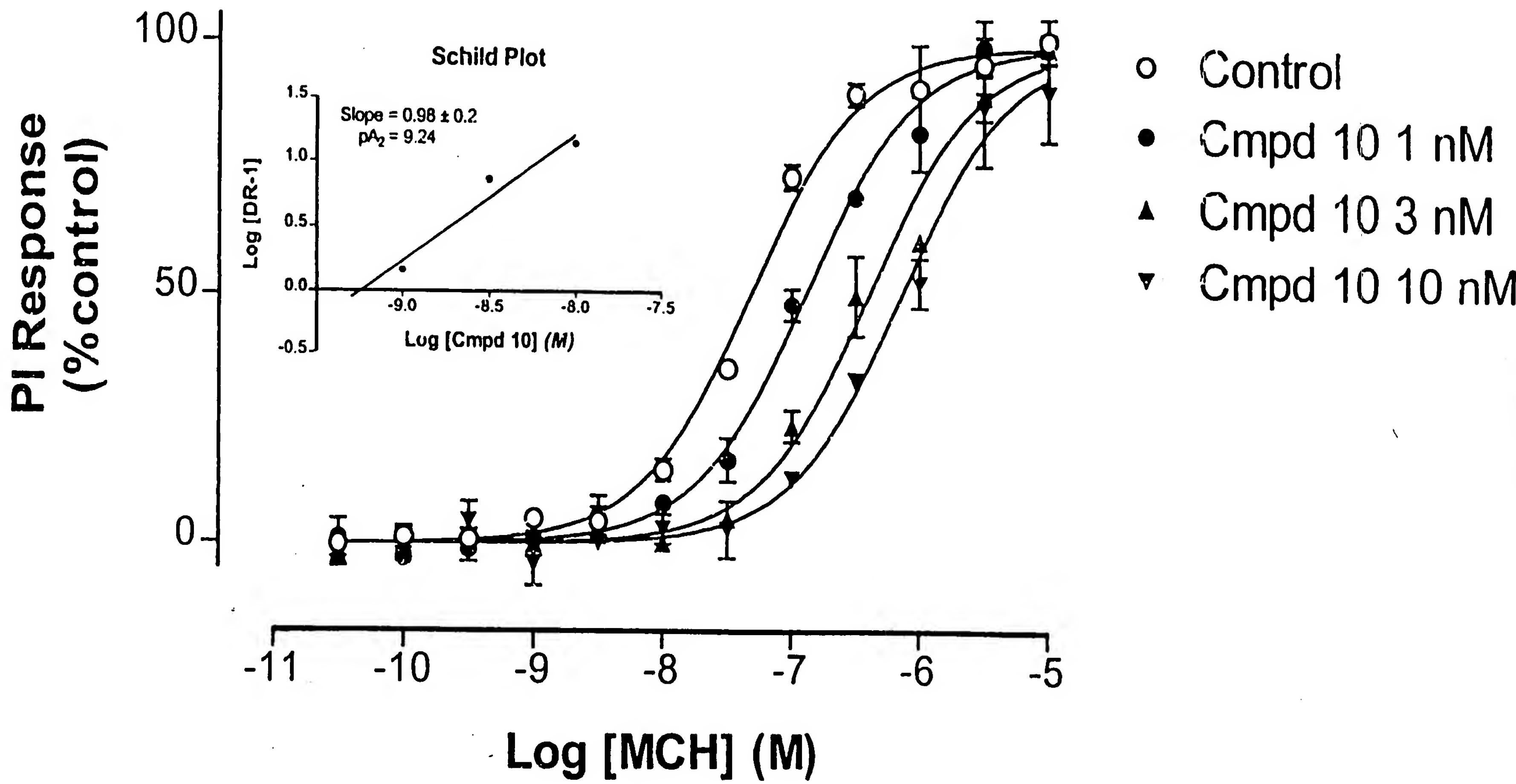
1	M	S	V	G	A	M	K	K	G	V	G	R	A	V	G	L	G	G	G	S	20
21	G	C	Q	A	T	E	E	D	P	L	P	D	C	G	A	C	A	P	G	Q	40
41	G	G	R	R	W	R	L	P	Q	P	A	W	V	E	G	S	S	A	R	L	60
61	W	E	Q	A	T	G	T	G	W	A	D	L	E	A	S	L	L	P	T	G	80
81	P	N	A	S	N	T	S	D	G	P	D	N	L	T	S	A	G	S	P	P	100
101	R	T	G	S	I	S	Y	I	N	I	I	M	P	S	V	F	G	T	I	C	120
121	L	L	G	I	I	G	N	S	T	V	I	F	A	V	V	K	K	S	K	L	140
141	H	W	C	N	N	V	P	D	I	F	I	I	N	L	S	V	V	D	L	L	160
161	F	L	L	G	M	P	F	M	I	H	Q	L	M	G	N	G	V	W	H	F	180
181	G	E	T	M	C	T	L	I	T	A	M	D	A	N	S	Q	F	T	S	T	200
201	Y	I	L	T	A	M	A	I	D	R	Y	L	A	T	V	H	P	I	S	S	220
221	T	K	F	R	K	P	S	V	A	T	L	V	I	C	L	L	W	A	L	S	240
241	F	I	S	I	T	P	V	W	L	Y	A	R	L	I	P	F	P	G	G	A	260
261	V	G	C	G	I	R	L	P	N	P	D	T	D	L	Y	W	F	T	L	Y	280
281	Q	F	F	L	A	F	A	L	P	F	V	V	I	T	A	A	Y	V	R	I	300
301	L	Q	R	M	T	S	S	V	A	P	A	S	Q	R	S	I	R	L	R	T	320
321	K	R	V	T	R	T	A	I	A	I	C	L	V	F	F	V	C	W	A	P	340
341	Y	Y	V	L	Q	L	T	Q	L	S	I	S	R	P	T	L	T	F	V	Y	360
361	L	Y	N	A	A	I	S	L	G	Y	A	N	S	C	L	N	P	F	V	Y	380
381	I	V	L	C	E	T	F	R	K	R	L	V	L	S	V	K	P	A	A	Q	400
401	G	Q	L	R	A	V	S	N	A	Q	T	A	D	E	E	R	T	E	S	K	420
421	G	T																			422

FIGURE 14

```
  1  M S V G A A K K G V G R A V G L G G G S  20
 21  G C Q A T E E D P L P D C G A C A P G Q  40
 41  G G R R W R L P Q P A W V E G S S A R L  60
 61  W E Q A T G T G W A D L E A S L L P T G  80
 81  P N A S N T S D G P D N L T S A G S P P  100
101  R T G S I S Y I N I I M P S V F G T I C  120
121  L L G I I G N S T V I F A V V K K S K L  140
141  H W C N N V P D I F I I N L S V V D L L  160
161  F L F G M P F M I H Q L M G N G V W H F  180
181  G E T M C T L I T A M D A N S Q F T S T  200
201  Y I L T A M A I D R Y L A T V H P I S S  220
221  T K F R K P S V A T L V I C L L W A L S  240
241  F I S I T P V W L Y A R L I P F P G G A  260
261  V G C G I R L P N P D T D L Y W F T L Y  280
281  Q F F L A F A L P F V V I T A A Y V R I  300
301  L Q R M T S S V A P A S Q R S I R L R T  320
321  K R V T R T A I A I C L V F F V C W A P  340
341  Y Y V L Q L T Q L S I S R P T L T F V Y  360
361  L Y N A A I S L G Y A N S C L N P F V Y  380
381  I V L C E T F R K R L V L S V K P A A Q  400
401  G Q L R A V S N A Q T A D E E R T E S K  420
421  G T                                    422
```

FIGURE 15

FIGURE 16



PI Response (%control)
100
50
0
Schild Plot
Slope = 0.98 ± 0.2
pA_2 = 9.24
Log [DR-1]
1.5
1.0
0.5
0.0
-0.5
-9.0
-8.5
-8.0
-7.5
Log [Cmpd 10] (M)
-11
-10
-9
-8
-7
-6
-5
Log [MCH] (M)
Control
Cmpd 10 1 nM
Cmpd 10 3 nM
Cmpd 10 10 nM

FIGURE 17

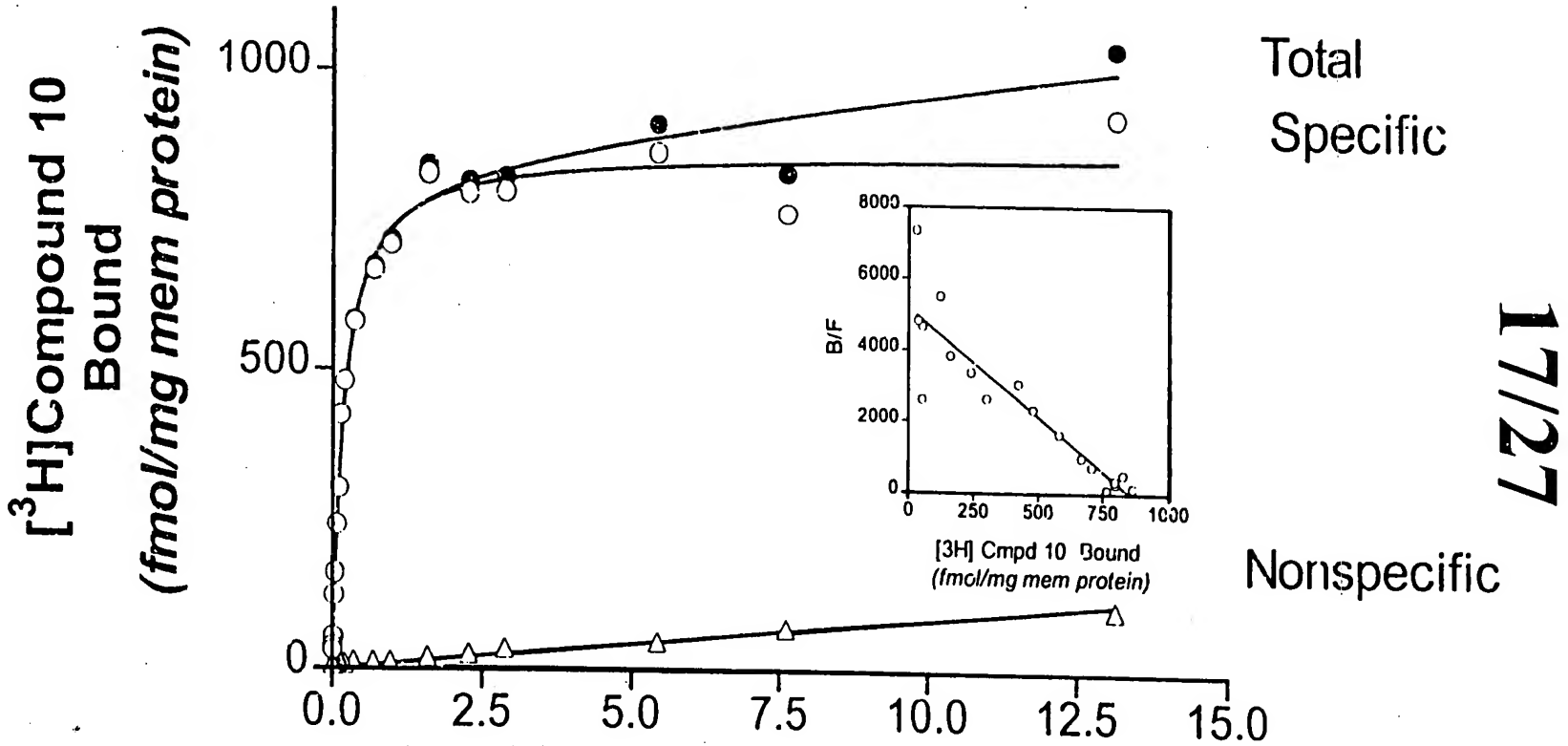


FIGURE 18

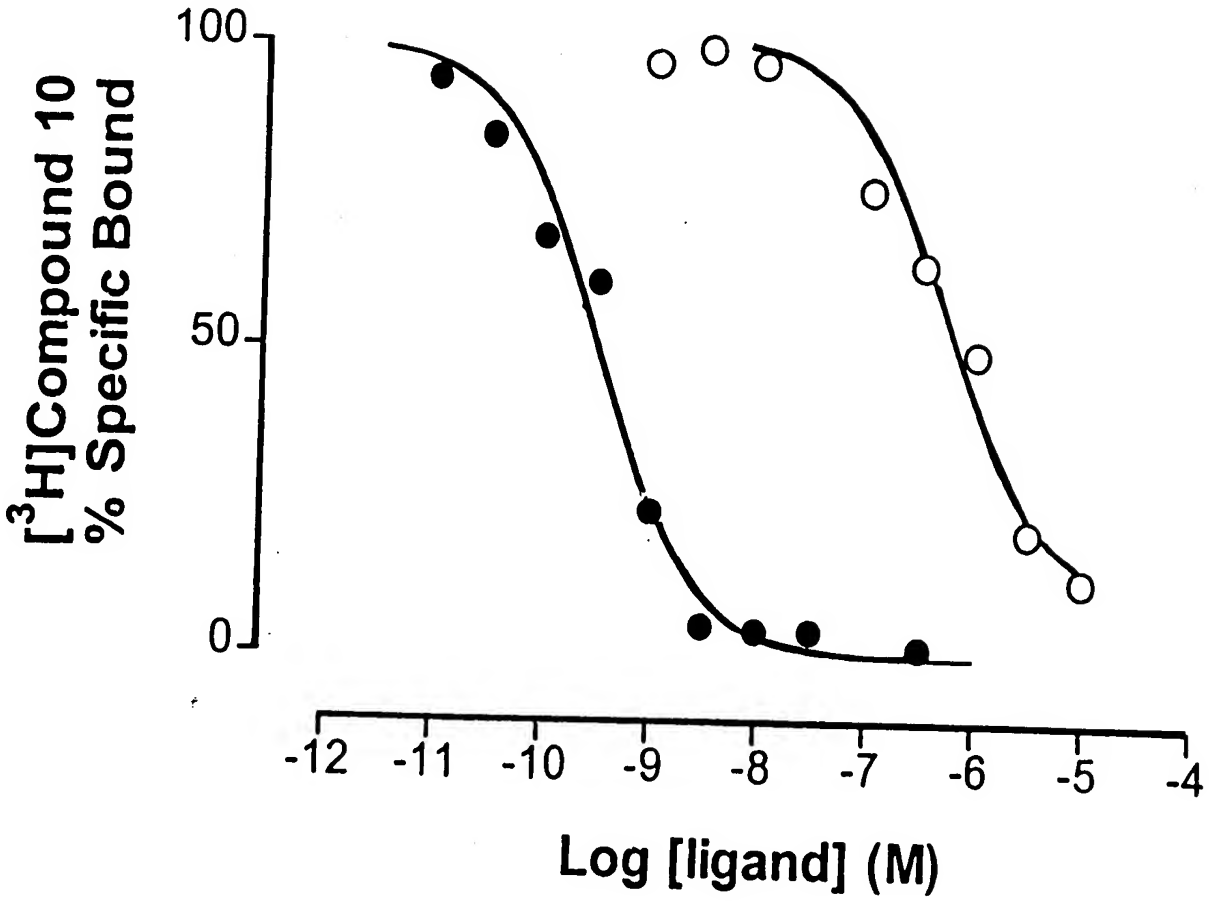


FIGURE 19

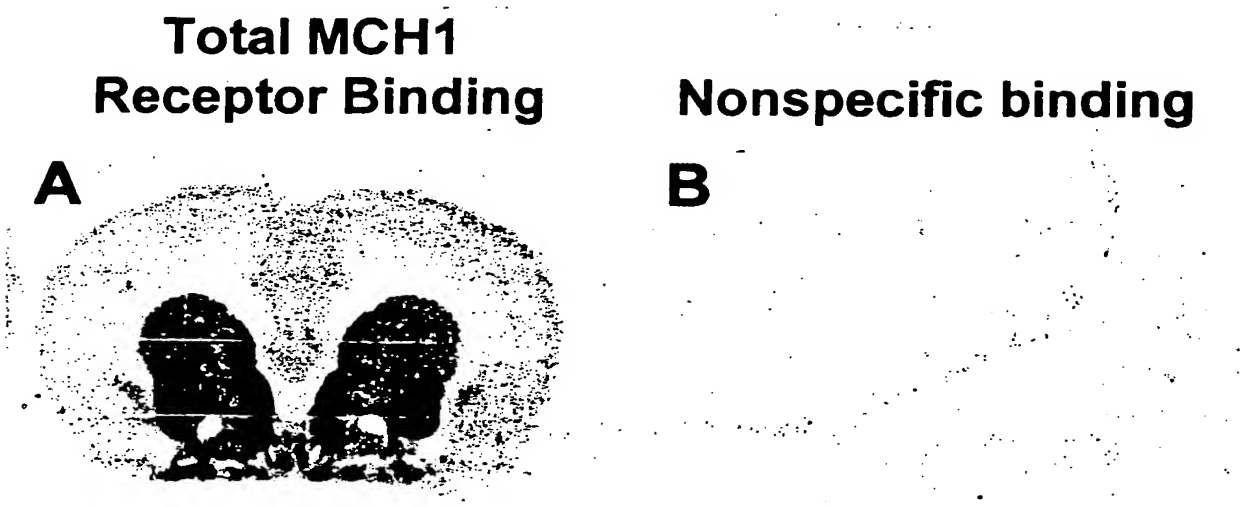


FIGURE 20A

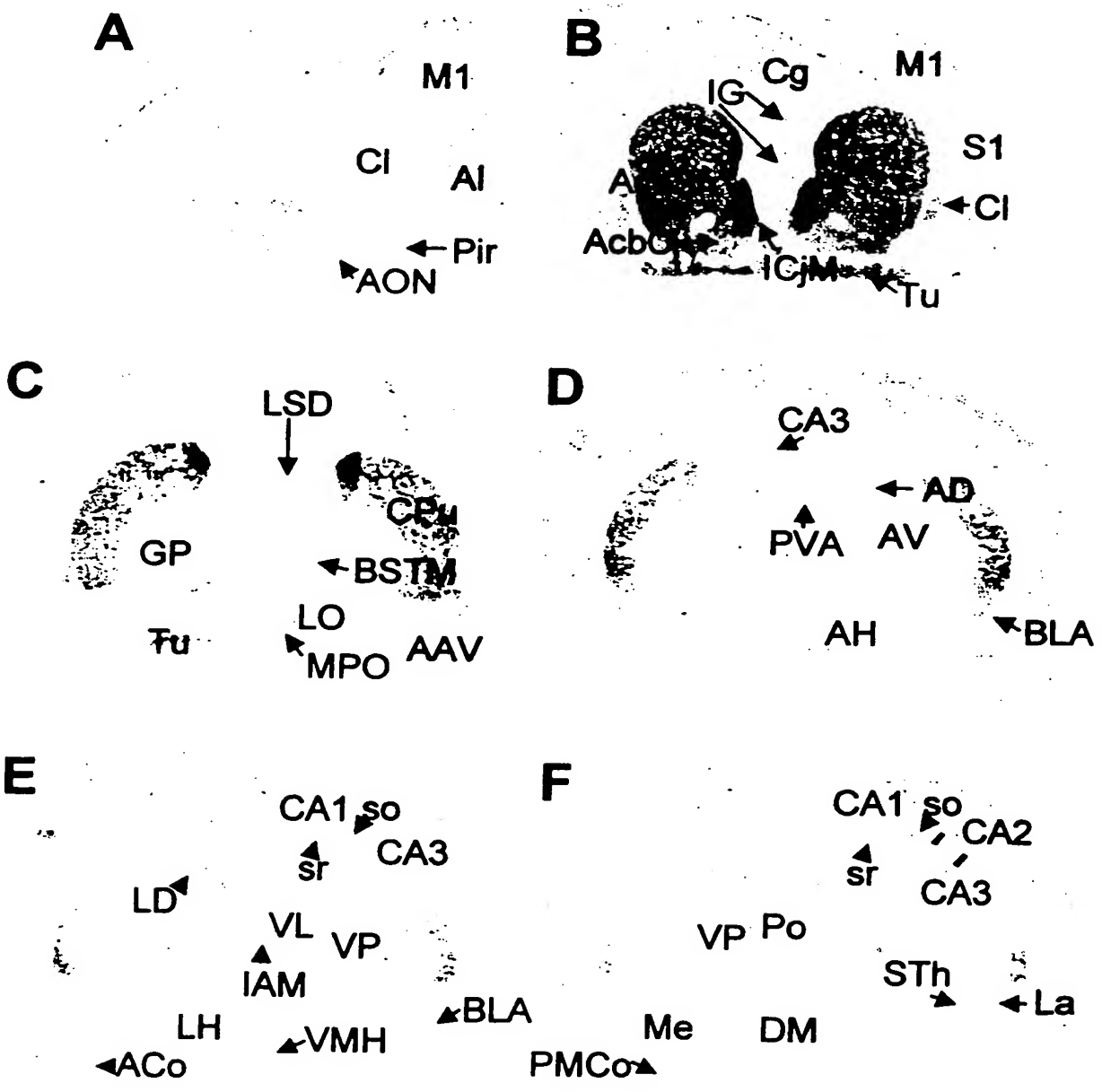

A
M1
Cl
Al
Pir
AON
B
Cg
M1
IG
S1
Cl
Tu
C
LSD
CPu
GP
BSTM
LO
Tu
MPO
AAV
D
CA3
AD
PVA
AV
AH
BLA
E
CA1
so
CA3
sr
LD
VL
VP
IAM
LH
VMH
BLA
ACo
F
CA1
so
CA2
sr
CA3
VP
Po
STh
La
Me
DM
PMCo

FIGURE 20B

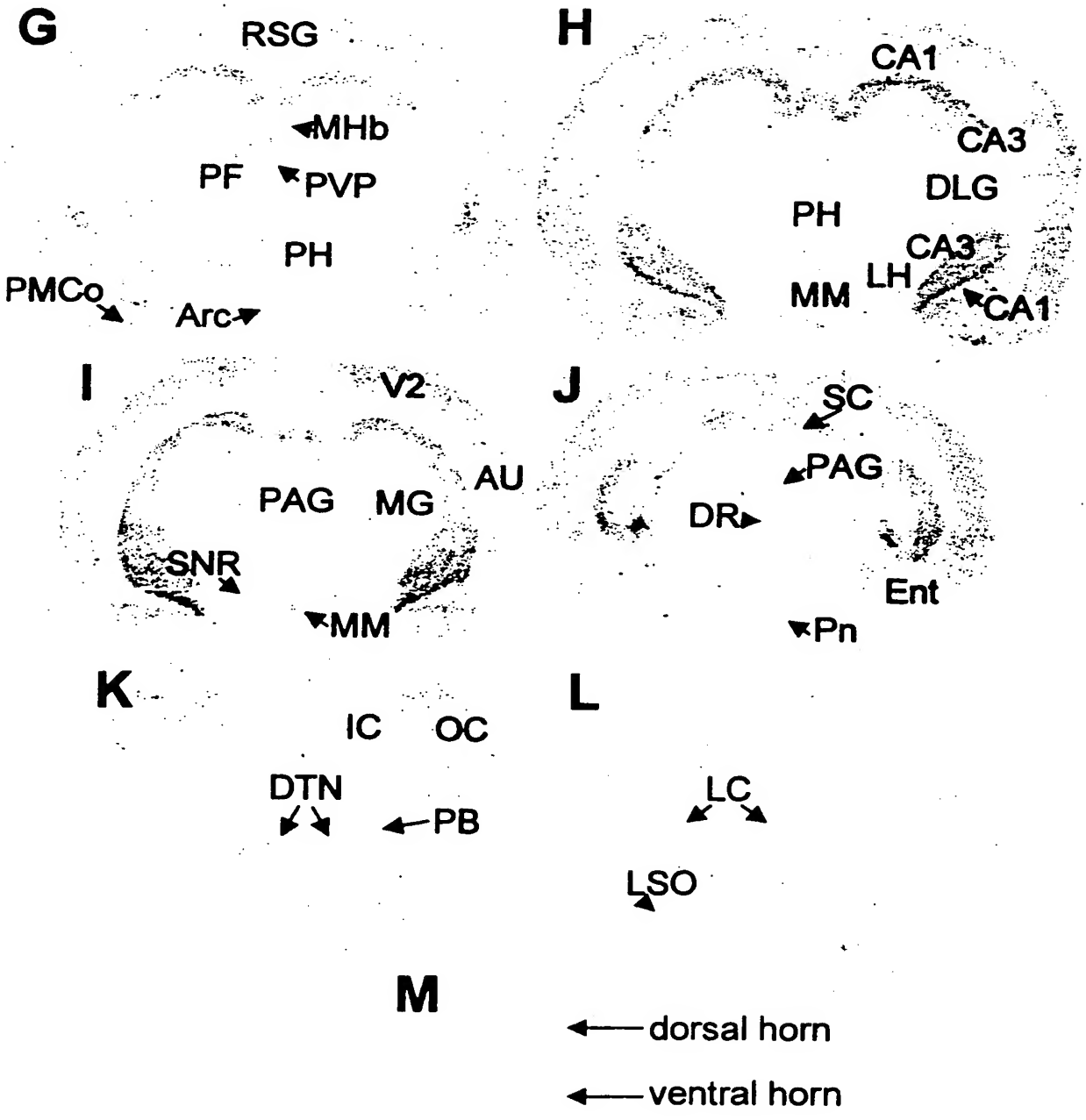
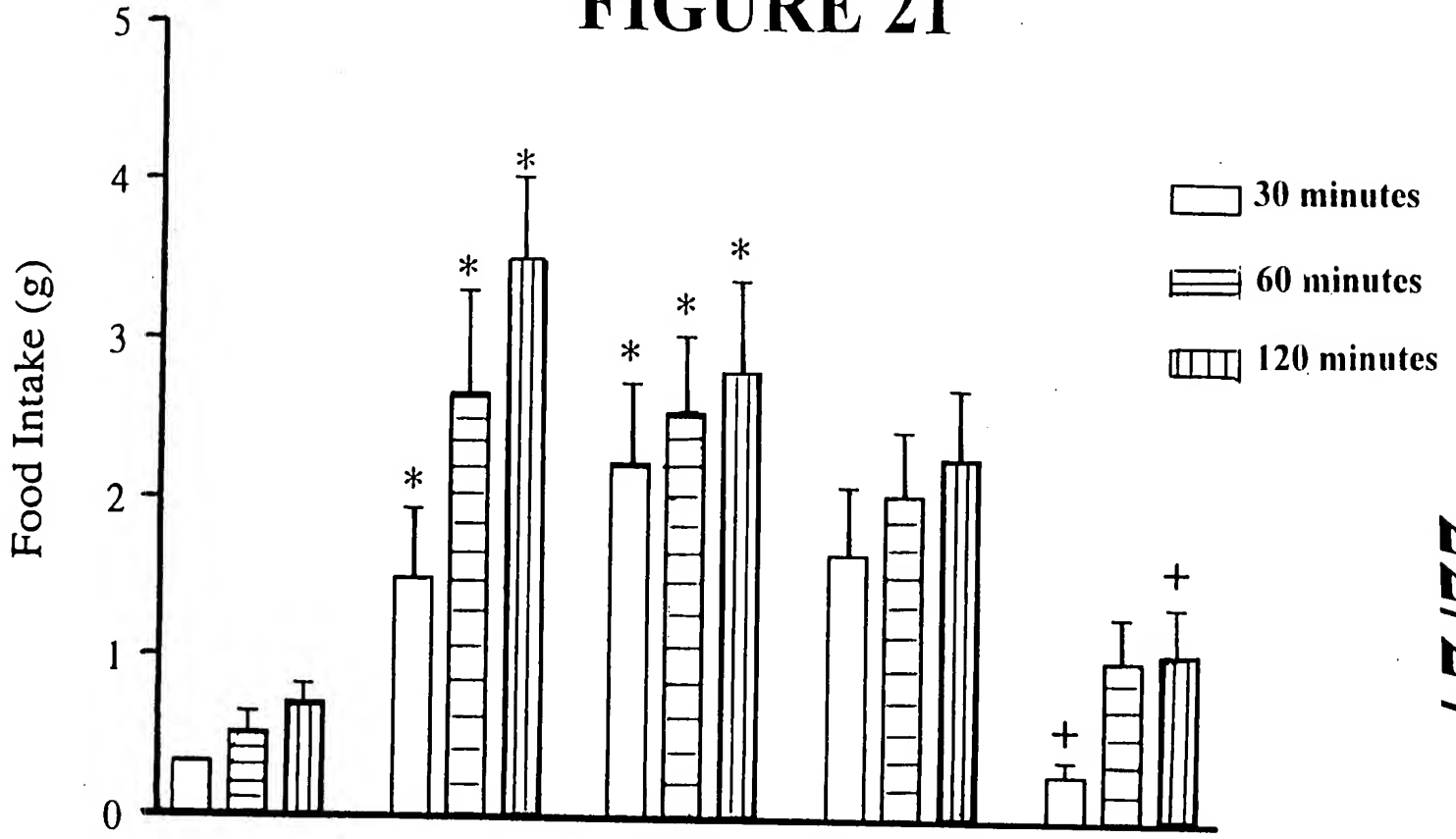


FIGURE 21



i.p. treatment:				**Vehicle**	**Comp 10 1 mg/kg ip**	**Comp 10 10 mg/kg ip**
i.c.v. treatment:	**Vehicle**	**MCH 3 nmol**	**MCH 3 nmol**	**MCH 3nmol**	**MCH 3nmol**

* sig. > than vehicle

\+ sig. < than veh+MCH

FIGURE 22

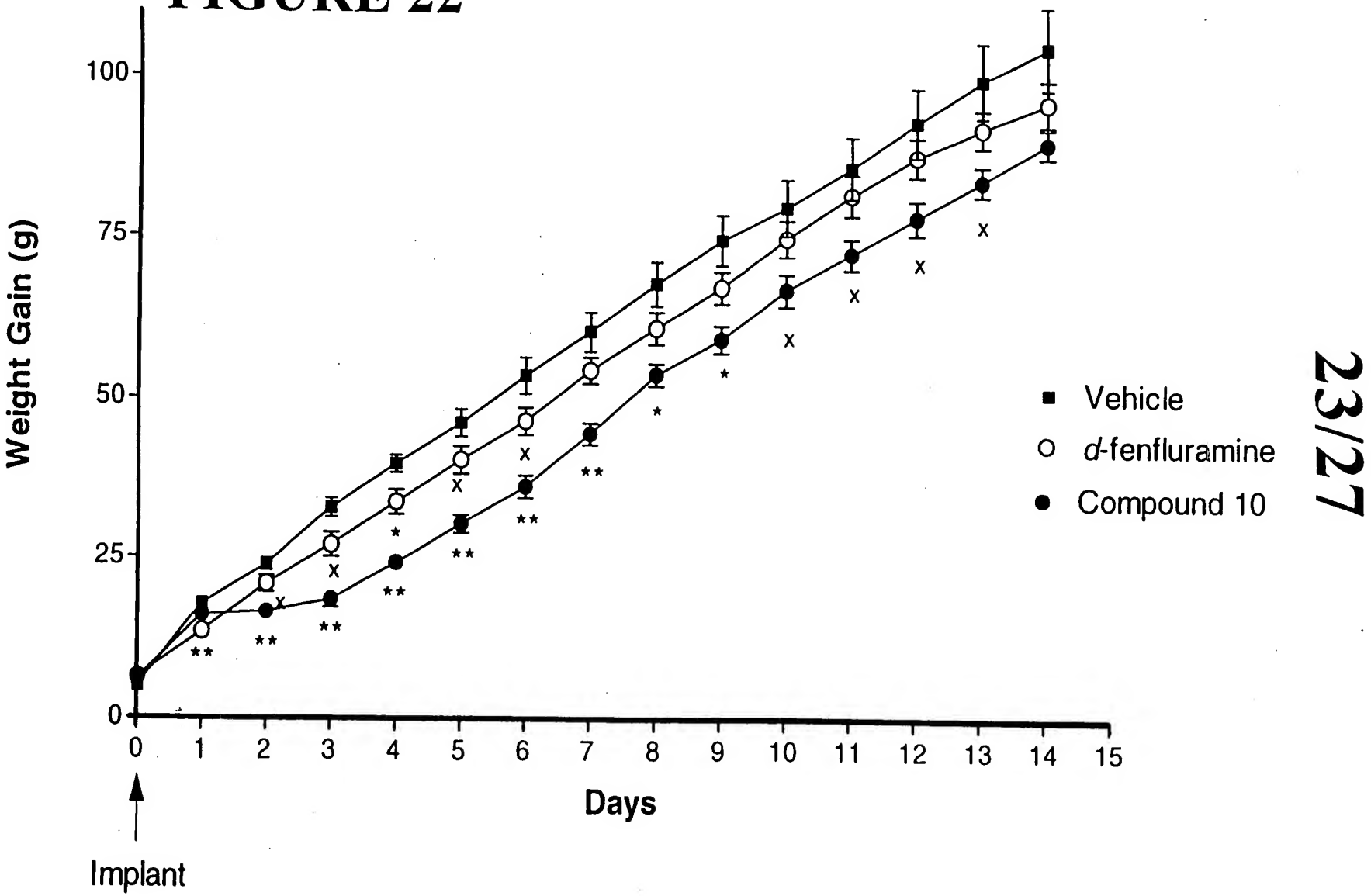

Weight Gain (g)
100
75
50
25
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days
Implant
Vehicle
d-fenfluramine
Compound 10

FIGURE 23

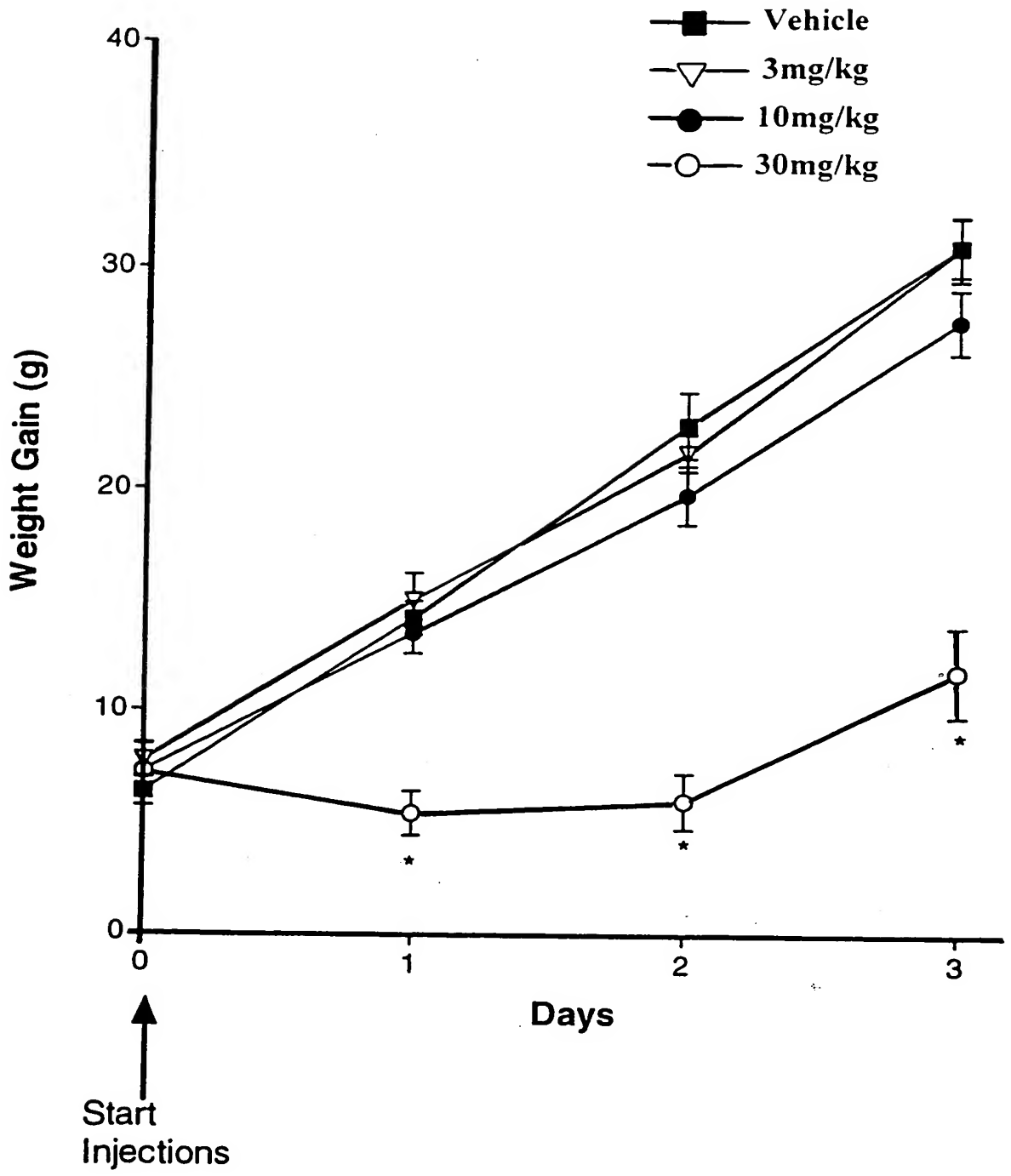


FIGURE 24

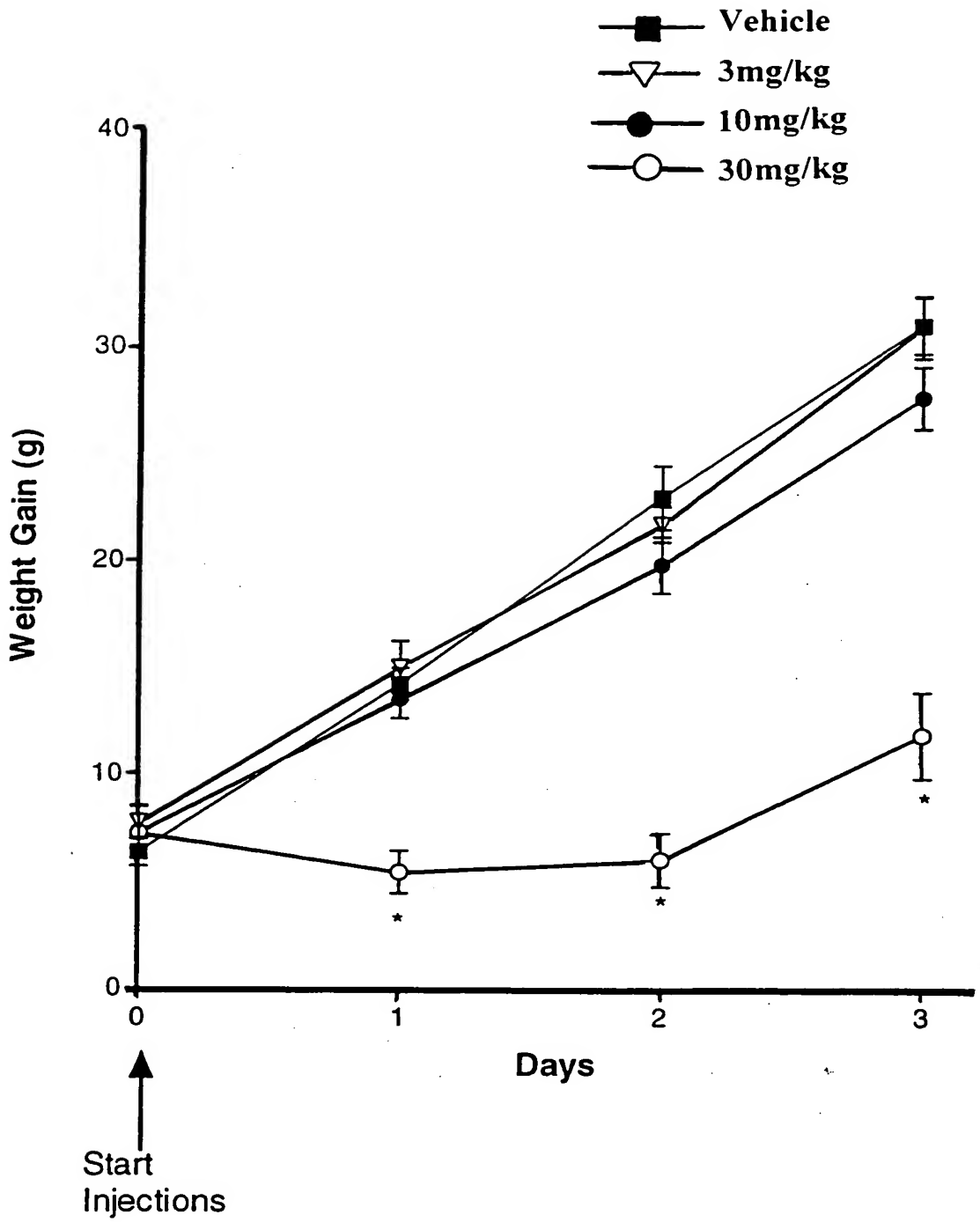

Vehicle
3mg/kg
10mg/kg
30mg/kg
Weight Gain (g)
40
30
20
10
0
0
1
2
3
Days
*
*
*
Start
Injections

FIGURE 25

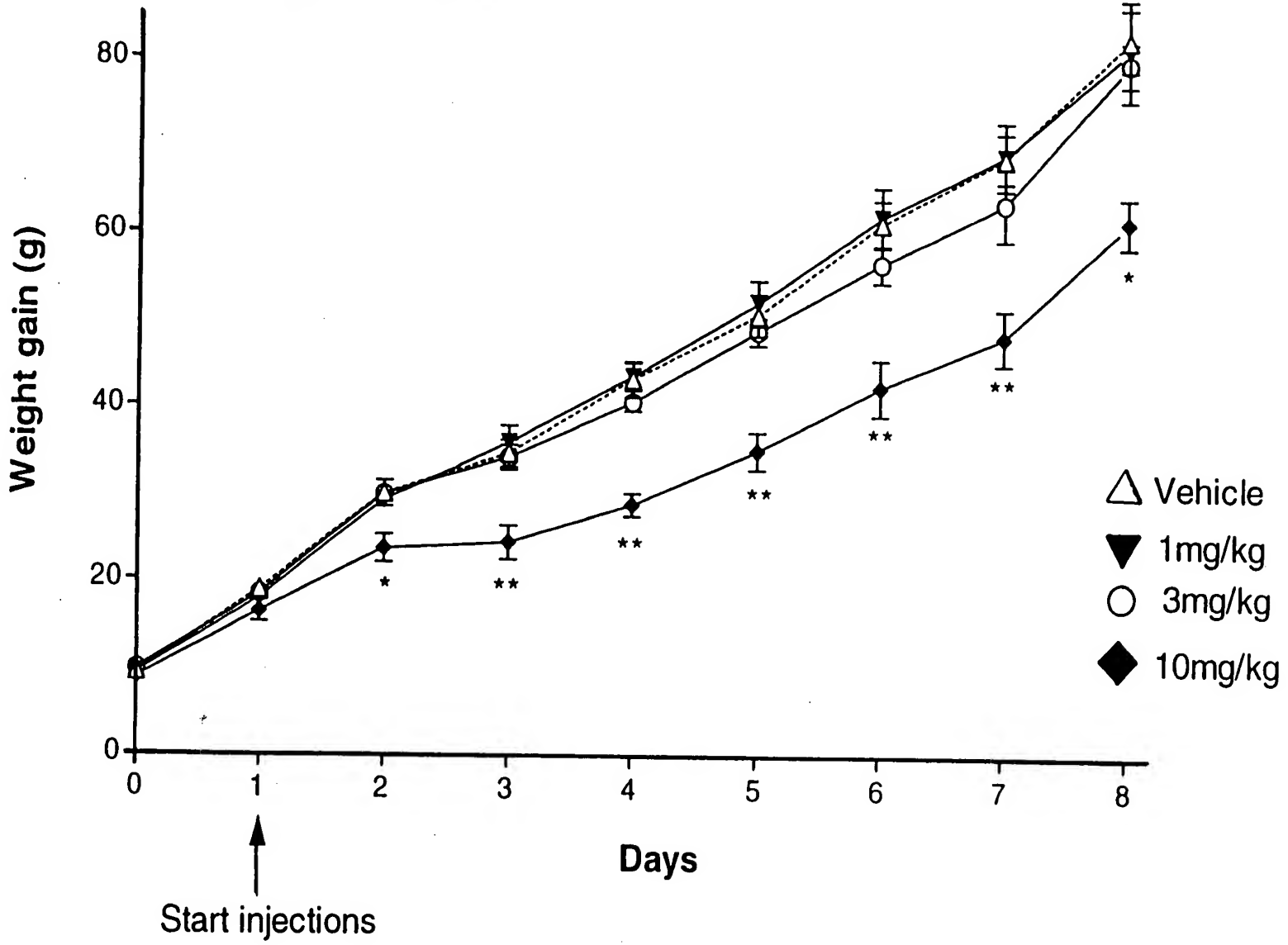
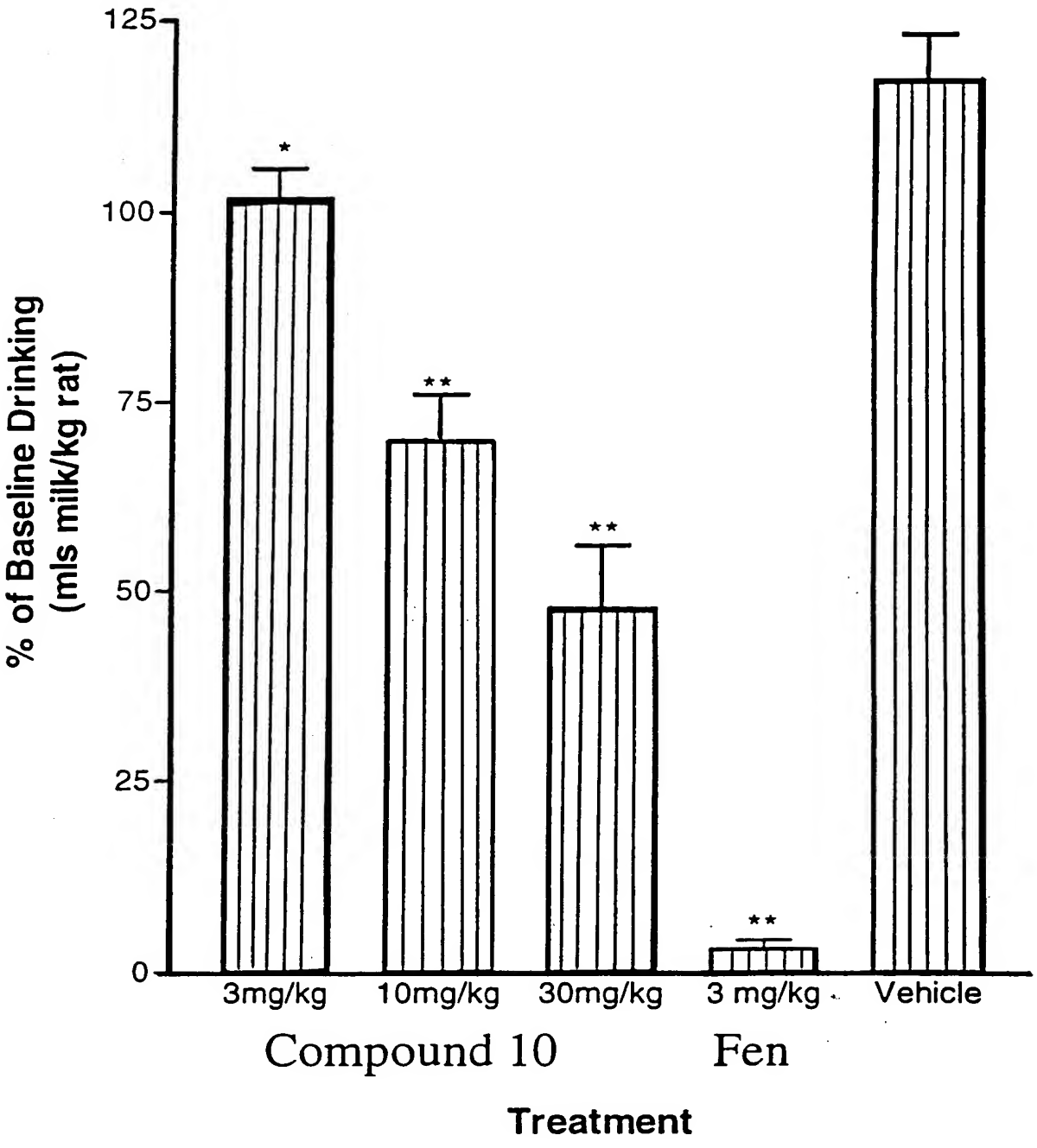

Weight gain (g)
80
60
40
20
0
0
1
2
3
4
5
6
7
8
Days
Start injections
Vehicle
1mg/kg
3mg/kg
10mg/kg
*
**

FIGURE 26


125
100
75
50
25
0
% of Baseline Drinking
(mls milk/kg rat)
*
**
**
**
3mg/kg
10mg/kg
30mg/kg
3 mg/kg
Vehicle
Compound 10
Fen
Treatment